21 October 1976

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Dear Francis,

     Thank you for all the new letters, particularly the correspondence
with Bak. I certainly is an exciting time and I very much like your
idea of the supersolenoid. I have called a chromatin meeting for this
Friday, at which Ashburner and Sidney will be present. I have already
had a word with Sidney, and he thinks your point (in your letter of
14 October) about translocations is a good one. I will write again
after the meeting at which the genetic implications will have been
discussed.

     On the supersolenoid itself, I have now found my notes on the
E.M. Meeting in Jerusalem, and Hans Ris definitely said that mitotic
chromosomes were formed by folding the 250 Å fibre into one of diameter
about 1000 - 2000 Å. However he did not present any pictures (his
slides were lost when his baggage was stolen at Paris Airport!) but
I suspect they would show the same sort of murky pictures as before,
and the idea of coiling into a thicker fibre is just a general one.
I doubt if he has any hard evidence, but he may have some estimates
of diameters from sections. This value may be a tricky one since
I would imagine that it could change fairly easily if the coils of
the supersolenoid were not held by ties. Your secondary idea of the
ties being preserved is a very neat one, but I wonder if it isn't all
oversimplified. Sidney thought it unlikely, but I do see the point of
the possible correlation between the smallness of Drosophila metaphase
chromosome and the smaller size of the genes.

     I have been looking at papers on the electron microscopy of
sectioned mitotic chromosomes and there is just no trace of a hollow
centre. There are many examples, but I enclose a reprint of an old
paper of Hugh's, see figure 14. Richard Skaer has also brought in some
much more recent photographs, and what one sees in transverse section
are fairly dense bodies about a micron across. Even allowing for the
possible double helical coiling at the next level, I think a hollow
tube would have been evident even if it had been considerably flattened.
Perhaps the lumen is filled with other proteins and possibly some
looser DNA. This last notion is distasteful as I think you are right
that the metaphase chromosome should have a compact, and therefore
regular, structure.

affects the way in which Bak has done his calculation of the contraction ratio. One minor point: perhaps you could change the reference to Bradbury in such a way that it is not cited as equal evidence with the paper by John and myself. I don't know if you have read the paper itself (Carpenter et al., July 1976, Nucleic Acids Research) but the level of significance of the "split peak" is barely above noise level. I personally don't think anyone could have deduced the existence of the solenoid, let alone the number of units per turn, from such pictures unless one knew what answer to expect. (Moreover, the key pattern was taken at 32% relative humidity, which corresponds to a concentration of over 60%.)

By the way, one other point which you don't mention explicitly, but must be obvious to you. If the interphase structure is to go continuously into the metaphase structure preserving the solenoids in the inactive genes, then I think your idea of DNA down the middle of a solenoid can't hold. I append a sketch illustrating the point. I have always favoured the situation (a) because of the fact that, in the original experiments in which we extracted (rather than reconstituted) solenoids in the presence of magnesium, they always looked curved.

Thank you also for your comments on the packing of the crystals. I can't think for what reason you suggested, in your letter of 11 October, that you liked a model in which the dyads were tilted in the AC plane. Indeed, I had something very like this in mind when I wrote in my letter that the ideal packing of columns, that I had proposed, would be perturbed. I draw a picture showing the general type of perturbation which indeed does account for the difference in the X-ray patterns looking down the 110 $\overset{o}{A}$ axis and the 192 $\overset{o}{A}$ axis. How did you derive it, unless you remembered the pictures themselves?! I am still not sure, but I think I have evidence for the approximate 120° rotation by considering the distribution of intensities, but more on that later. In any case, I am not sure how your particular detailed model would relate to the packing in a solenoid. Why would tilts of 30° be required for this?

More soon,

Yours ever,

A. Klug

Encs.